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LAG-3 IMMUNOTHERAPY

# TACTI-003 Topline Data Update for Patients with Any PD-L1 Expression (Cohort A) & Negative PD-L1 Expression (Cohort B) in 1L HNSCC and Overview of TACTI-004 Pivotal Phase III in 1L NSCLC

Global Webcast Presentation – Thursday, June 27th, at 9AM AEST (Wednesday, June 26th, at 7PM ET)

# Forward-Looking Statements

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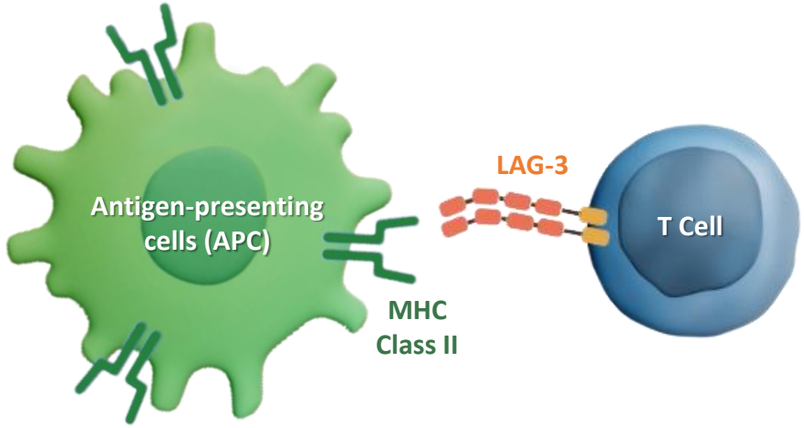
# Pioneering LAG-3 Immunotherapy Portfolio




Immutep has designed multiple first-in-class therapeutics targeting either **MHC Class II molecules** on antigen-presenting cells (APC) or **LAG-3** on T-cells to fight cancer & autoimmune disease

## Targeting MHC Class II on APCs#

**Efti**
Soluble LAG-3 fusion protein

**Oncology**
Immune Stimulation

## Targeting LAG-3 on T cells

**LAG525***
Blocking LAG-3 antibody

Anti-LAG-3 small molecule

**Oncology**
Immune Stimulation

**GSK'781***
Depleting LAG-3 antibody

**IMP761**
Agonist LAG-3 antibody

**Autoimmune Disease**
Immune Suppression



# MHC Class II = Major Histocompatibility Complex Class II. * LAG525 (leramilimab) is out-licensed to Novartis. The clinical-stage asset, GSK'781 is being transitioned back to Immutep as the licensing agreement has been terminated with an effective date of 30 May 2024.

# Deep LAG-3 Pipeline in Oncology & Autoimmune Diseases

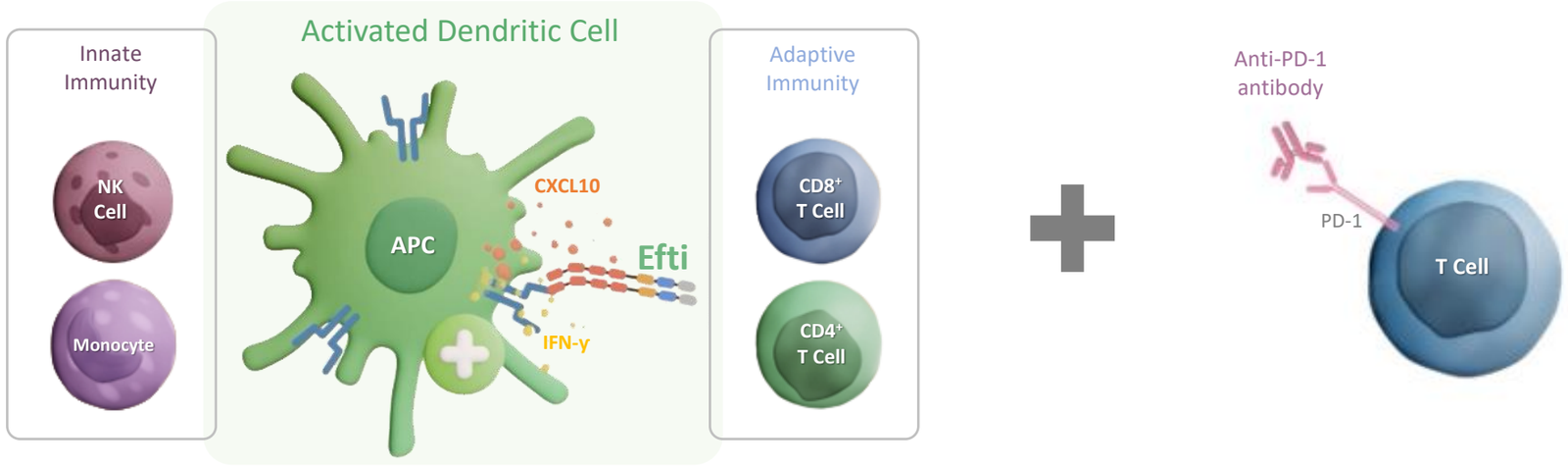
| | Program | Indication | Preclinical | Phase I | Phase II | Late Stage# | Collaborations | Commercial Rights |
|---|---|---|---|---|---|---|---|---|
| ONCOLOGY | **Eftilagimod Alpha**<br>Soluble LAG-3 Protein & MHC Class II agonist | 1L Non-Small Cell Lung Cancer (NSCLC) | TACTI-004 \| Efti + Pembrolizumab + Chemo [a] | | | | MERCK | immutep Global Rights ex-China |
| | | 1L Head & Neck Squamous Cell Carcinoma (HNSCC) | TACTI-003 \| Efti + Pembrolizumab [a] | | | | MERCK | |
| | | 1L NSCLC, 2L HNSCC, PD-X Refractory 2L NSCLC | TACTI-002 \| Efti + Pembrolizumab [a] | | | | MERCK | |
| | | 1L Non-Squamous NSCLC | INSIGHT-003 \| Efti + Pembrolizumab + Chemo [§] | | | | IKF | |
| | | Urothelial Cancer | INSIGHT-005 \| Efti + Avelumab [§, b] | | | | Merck KGaA Darmstadt, Germany; IKF | |
| | | Soft Tissue Sarcoma | EFTISARC-NEO \| Efti + Pembro + Radiotherapy [§] | | | | Narodowy Instytut Onkologii | |
| | | HR+/HER2- Metastatic Breast Cancer & TNBC | AIPAC-003 \| Efti + Paclitaxel | | | | | |
| | | Metastatic Breast Cancer & Solid Tumors | Efti + Paclitaxel and Efti + Pembrolizumab [##] | | | | EOC | EOC Efti China Rights |
| | Anti-LAG-3 Small Molecule | Undisclosed | | | | | CARDIFF UNIVERSITY | immutep Global Rights |
| | **LAG525**<br>Anti-LAG-3 Antibody | Solid Tumors & Blood Cancer | | | | | NOVARTIS | NOVARTIS Global Rights |
| | | Triple Negative Breast Cancer | | | | | | |
| | | Melanoma | | | | | | |
| | | Solid Tumors | | | | | | |
| | | Triple Negative Breast Cancer | | | | | | |
| AUTOIMMUNE DISEASE | **IMP731*** Depleting LAG-3 Antibody | Ulcerative Colitis | | | | | | immutep Global Rights |
| | | Psoriasis | | | | | | |
| | | Healthy Subjects | | | | | | |
| | **IMP761**** Agonist LAG-3 Antibody | Undisclosed | | | | | | |

Information in pipeline chart current as of June 2024. For EOC's China rights, Immutep may receive undisclosed milestones plus royalties; LAG525 (ieramilimab)- ClinicalTrials.gov (for Novartis' global rights, Immutep may receive milestones plus royalties); Immutep has no control over the trials.

§ Investigator Initiated Trials controlled by lead investigator & therefore Immutep has no control over these clinical trials. [a] In combination with KEYTRUDA®. [b] In combination with BAVENCIO®. # Late stage refers to active Phase IIb clinical trials or more clinically advanced clinical trials. ## Conducted by EOC in China.* IMP731 - The clinical-stage asset GSK'781 is being transitioned back to Immutep as the licensing agreement has been terminated with an effective date of 30 May 2024. ** IMP761 – Phase I study to launch mid-CY2024.

# Differentiated Approach in Oncology

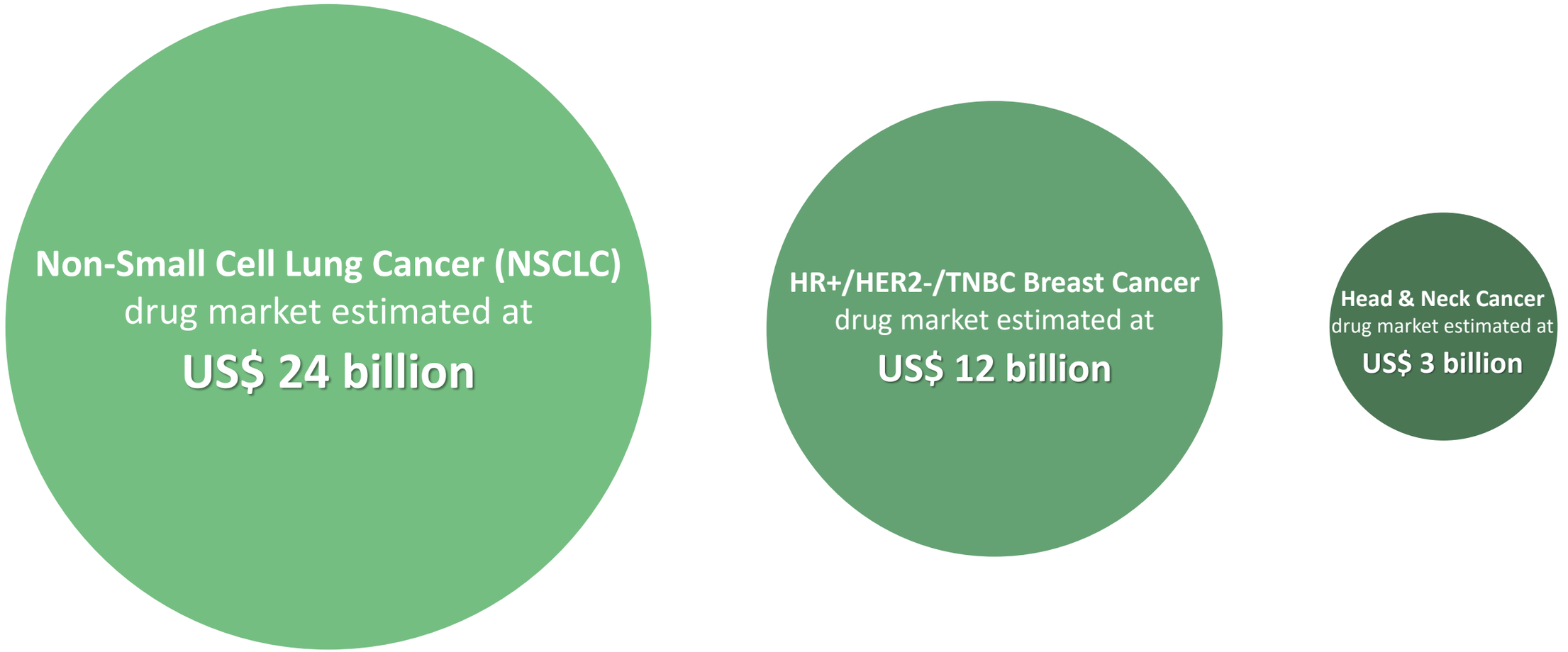
*Efti has complementary action with immune checkpoint inhibitors (ICIs) like anti-PD-(L)1 therapy*




**Efti's unique activation of antigen-presenting cells (e.g. dendritic cells, monocytes) engages the adaptive and innate immune system, which complements anti-PD-(L)1 therapy to fight cancer**

- Efficacy across "hot", "tepid", "cold" tumours in patients with high, low, negative PD-L1 expression
- Additionally, efti in combination with anti-PD-(L)1 has a favourable safety profile

# Clinical Trials Target Large Addressable Markets




*Efti has FDA Fast Track designation in 1L NSCLC and 1L HNSCC

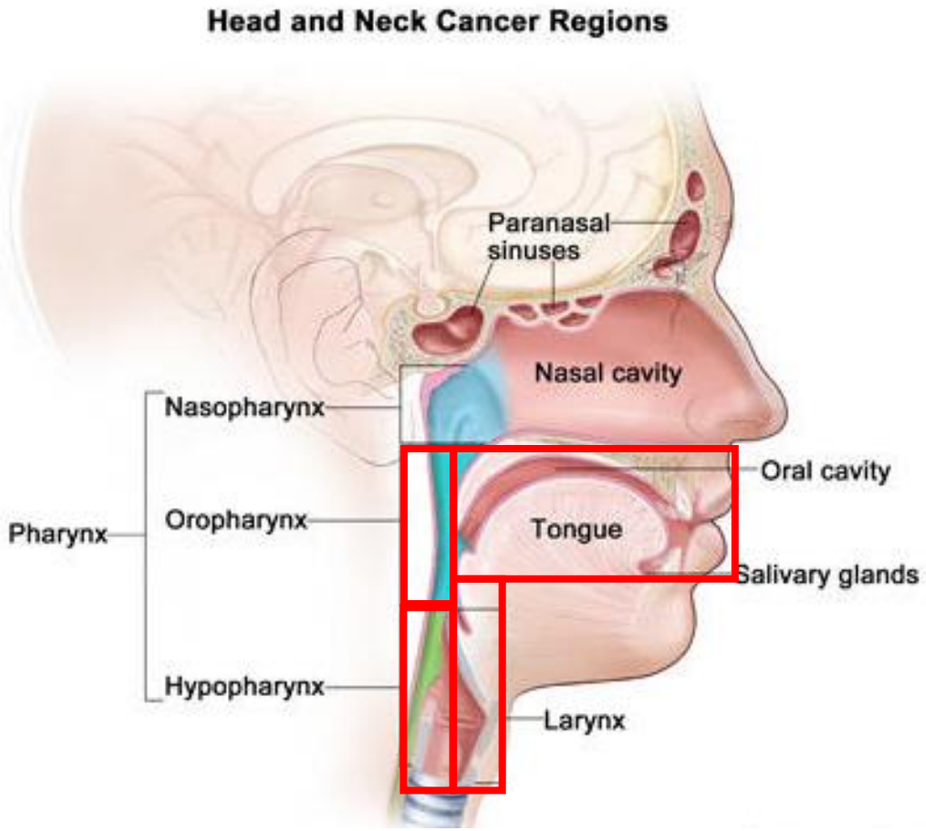


Market size estimates are based on intelligence data extracted from GlobalData in June 2024 (estimations 2024 for 8MM: FR, DE, IT, JP, ES, UK, US, China), and Nature Reviews Drug Discovery 22, 264-265 (23 Jan 2023) doi: https://doi.org/10.1038/d41573-023-00017-9

# TACTI-003

First Line Head & Neck Squamous Cell Carcinoma (1L HNSCC)

# Head and Neck Squamous Cell Carcinoma




TACTI-003 included cancers that originate from the areas delineated by red boxes

## Overview:

- Head and neck squamous cell carcinoma (HNSCC) encompasses a spectrum of heterogeneous diseases originating in the oral cavity, pharynx, and larynx
- HNSCC is a complex disease involving distinct anatomical sites and with varying etiological factors including smoking, alcohol consumption and infection with Human Papilloma Virus (HPV)

## Epidemiology:

- More than 890,000 HNSCC diagnoses and 450,000 deaths per annum worldwide[1]
- Up to ~100,000 estimated to develop metastatic disease in 8MM countries[2]
- 5-year survival for metastatic HNSCC is 39.3%[3] and varies depending on the anatomical site of cancer origin



 (1) Johnson, D.E., Burtness, B., Leemans, C.R. et al. Head and neck squamous cell carcinoma. Nat Rev Dis Primers 6, 92 (2020). https://doi.org/10.1038/s41572-020-00224-3. (2) Extracted from GlobalData in June 2024, 8 Major Markets (8MM): US, China, Japan, France, Germany, Italy, Spain, UK. (3) Epidemiology, Risk Factors, and Prevention of Head and Neck Squamous Cell Carcinoma. Barsouk et. al. Med Sci (Basel). 2023 Jun; 11(2): 42.

# Treatment Landscape in 1L HNSCC

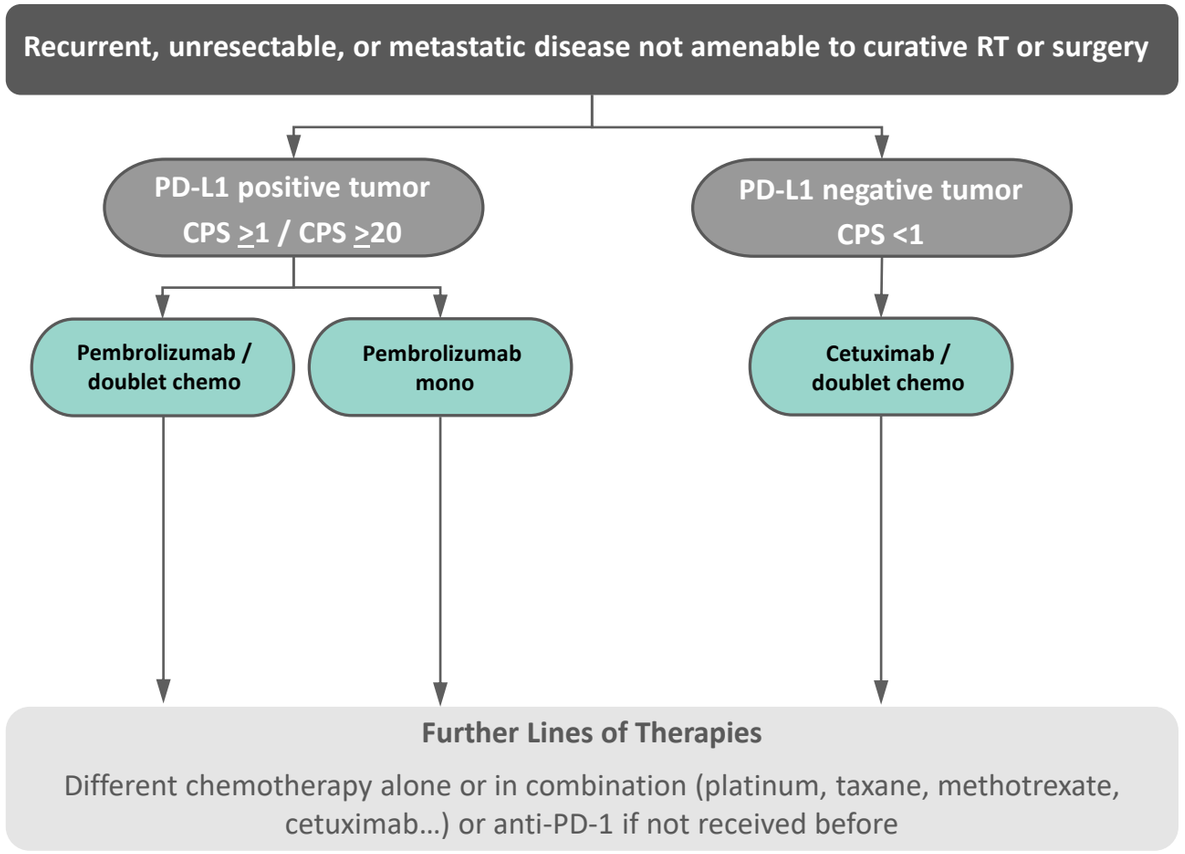
## High unmet need:

- Overall Survival in first line HNSCC is ~12 months

## PD-L1 expression:

- PD-L1 expression as measured by Combined Proportion Score (CPS) is an FDA approved predictive biomarker in 1L HNSCC for anti-PD-1 therapy
- Patients are grouped by high (CPS ≥20), low (CPS 1-19), and negative (CPS <1) PD-L1 expression[1]. Generally, high PD-L1 expressors respond best, low respond sub-optimally, and negative have negligible responses to anti-PD-1 therapies.
- Currently, there are no effective chemotherapy-free treatments for patients with negative PD-L1 expression

**High unmet medical need for well tolerated and efficacious treatment options**



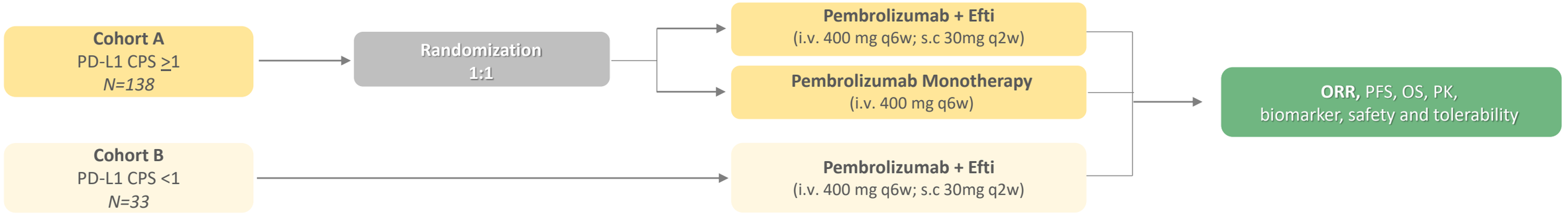

Simplified based on NCCN Guidelines Head and Neck Cancers and EHNS-ESMO-ESTRO Clinical Practice Guidelines



The Food and Drug Administration (FDA) approved pembrolizumab in combination with ChT as first-line treatment regardless of PD-L1 expression and pembrolizumab alone for patients with PD-L1-expressing tumours (CPS ≥1). In contrast, the European Medicines Agency (EMA) has approved pembrolizumab with or without ChT only for patients with a CPS ≥1. Source: DOI:https://doi.org/10.1016/j.annonc.2020.07.011

# TACTI-003 / KEYNOTE-PNC-34 Trial Overview

*Efti + anti-PD-1 therapy has FDA Fast Track designation in recurrent or metastatic 1L HNSCC*




- Randomized, multicenter Phase IIb trial evaluating efti in combination with pembrolizumab (KEYTRUDA®) in first line recurrent or metastatic head and neck squamous cell carcinoma (1L HNSCC). A total of 171 patients enrolled in 29 clinical sites across nine countries (US, UK, ES, UA, AU, RO, UA, DK, DE):
  - *Cohort A (N=138) - Patients with any PD-L1 expression (CPS ≥1) randomized 1:1 evaluating efti + KEYTRUDA® versus KEYTRUDA monotherapy*
  - *Cohort B (N=33) - Patients with negative PD-L1 expression (CPS <1), which could not be randomized as KEYTRUDA monotherapy is not approved in CPS <1*
- Primary endpoint is Overall Response Rate (ORR) among evaluable patients (>= 1 post baseline CT), according to RECIST1.1
- Secondary endpoints include Overall Survival and Progression-Free Survival, ORR (iRECIST), and Disease Control Rate



The Food and Drug Administration (FDA) approved pembrolizumab in combination with ChT as first-line treatment regardless of PD-L1 expression and pembrolizumab alone for patients with PD-L1-expressing tumours (CPS ≥1). In contrast, the European Medicines Agency (EMA) has approved pembrolizumab with or without ChT only for patients with a CPS ≥1. Source: DOI:https://doi.org/10.1016/j.annonc.2020.07.011. Approval based on KN-048. Immutep conducts this clinical trial and has a clinical trial collaboration and supply agreement with Merck & Co., Inc., Kenilworth, NJ, USA (known as MSD outside the US and Canada).

# TACTI-003 Baseline Characteristics in Evaluable Patients

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- **149 evaluable patients** out of 171 patients enrolled*:
  - ✓ Efti + KEYTRUDA with CPS ≥1: 58 of 69 (84%)
  - ✓ KEYTRUDA alone with CPS ≥1: 60 of 68 (88%)
  - ✓ Efti + KEYTRUDA with CPS < 1: 31 of 33 (94%)
- Patients recruited **irrespective of HPV status & PD-L1 expression**
- CPS used for randomization/enrollment was assessed locally (65.8%) / centrally (34.2%)**
- Data read-out according to protocol with minimum follow-up of 18 weeks
- Data collection for follow up and additional analyses is ongoing, as well as for secondary endpoints

**Detailed presentation of TACTI-003 data (Cohorts A & B) planned for medical conferences in H2 of 2024**


Data cut-off date: March 11, 2024. Evaluable patient with ≥1 evaluable post-baseline scan * One patient (of the 171) has been enrolled, but never treated, therefore not part of analysis dataset. **CPS assessed with FDA-approved kit (IHC 22C3 pharmDx).

# Prognostic Factors in HNSCC

*Imbalances in treatment arms (e.g. smoking status, location of primary tumour) favour KEYTRUDA monotherapy arm*

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| Good | Prognosis | Poor | Imbalances in TACTI-003 (Cohort A) |
|---|---|---|---|
| Younger age | Age at onset | Older age | - None - |
| Female | Gender | Male | Favours KEYTRUDA arm (30.0% female vs 20.7% in combination arm) |
| 0 | Performance Status (ECOG) | 1 | - None - |
| Never, quitters | Smoking status | Current | Favours KEYTRUDA arm (16.7% current vs 22.4% in combination arm) |
| Other sites | Site of primary tumour | Hypopharynx | Favours KEYTRUDA arm (13.3% hypopharynx vs 19.0% in combination arm) |
| HPV+ | HPV status* | HPV- | Favours KEYTRUDA arm (65.0% HPV+ vs 29.2% in combination arm) |
| Stage I/II | Stage of cancer | Stage III/IV | - None - |
| Local in H&N area | Site of recurrence | Distant metastasis | - None - |
| Absent | Liver metastasis | Present | - None - |

* In patients with primary oropharyngeal tumors

- Multiple prognostic markers **favor the KEYTRUDA mono arm** (e.g., gender, smoking, HPV+/-, site of primary tumour)
- None of the prognostic markers favor the Efti + KEYTRUDA combination arm


References: (1) HPV: Fakhry et al, JCO 2014;32(30):3365-73; (2) Smoking cessation: Lee et al, Cancer 2023; 129:867-77; (3) Prognostic model: Argiris et al, EJC 2024.

# Safety

| Safety Parameter | Efti + KEYTRUDA (Cohorts A+B) n (%) | KEYTRUDA alone (Cohort A) n (%) |
|---|---|---|
| **Any TEAE Leading to Discontinuation of Study Treatment** | 8 (7.8%) | 4 (5.9%) |
| Related to Efti and/or Pembrolizumab | 6 (5.9%) | 3 (4.4%) |

- **No new safety signals**
- **Rate of treatment related discontinuation was low and comparable between treatment regimens**
- **Safety profile comparable to KEYTRUDA monotherapy**
- **More details will be shown at conference in H2 2024**


Data cut-off date: March 11, 2024

# Overall Response Rate in Evaluable Patients

*TACTI-003 primary endpoint is overall response rate (ORR) in evaluable patients, according to RECIST1.1*

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**Efti plus KEYTRUDA achieved a ~34% ORR regardless of PD-L1 levels and HPV status, including patients with negative PD-L1 expression**

"The strong, consistent response rates, irrespective of whether patients have high, low, or negative PD-L1 expression, is intriguing and offers a glimpse into this novel combination's ability to improve patients' clinical responses and expand patient populations that benefit from anti-PD-1 therapy."

*- Dr. Martin Forster, UCL Cancer Institute, London, UK*

**Efti plus KEYTRUDA led to higher ORR across all levels of PD-L1 expression versus KEYTRUDA monotherapy and durability is tracking well**

"We are pleased with the quality of responses. Once again, durability is tracking well driven by the complementary nature of these two unique immunotherapies in fighting cancer."

*- Dr. Frédéric Triebel, CSO of Immutep*



Data cut-off date: March 11, 2024
Evaluable patient with ≥1 evaluable post-baseline scan

# Randomised Cohort A in Patients with Any PD-L1 Expression

| | TACTI-003 | |
|---|---|---|
| | Efti + KEYTRUDA | KEYTRUDA alone |
| **High PD-L1 Expression (CPS ≥20)** | **31.0% ORR (N=29)** | **18.5% ORR (N=27)** |
| In CPS ≥20, efti + KEYTRUDA shows strongest outperformance with 68% relative increase and 12.5% absolute increase. Patients with CPS ≥20 represent ~50% of the 1L HNSCC patient population.* | | |
| **Low PD-L1 Expression (CPS 1-19)** | **34.5% ORR (N=29)** | **33.3% ORR (N=33)** |
| In CPS 1-19, efti + KEYTRUDA has relatively high 34.5% ORR in CPS 1-19. KEYTRUDA monotherapy's 33.3% ORR is higher than historical published data, including a 14.5% ORR in KN-048*, that may be explained by imbalances including gender, smoking status, HPV+/- status, and location of primary tumour. | | |
| **Any PD-L1 Expression (CPS ≥1)** | **32.8% ORR (N=58)** | **26.7% ORR (N=60)** |
| In CPS ≥1, efti + KEYTRUDA has 23% relative Increase and 6.1% absolute increase against KEYTRUDA monotherapy results that were driven higher by results in CPS 1-19 group.<br>efti + KEYTRUDA 90% CI: 22.6%-44.3%; KEYTRUDA 90% CI: 17.5%-37.6% | | |



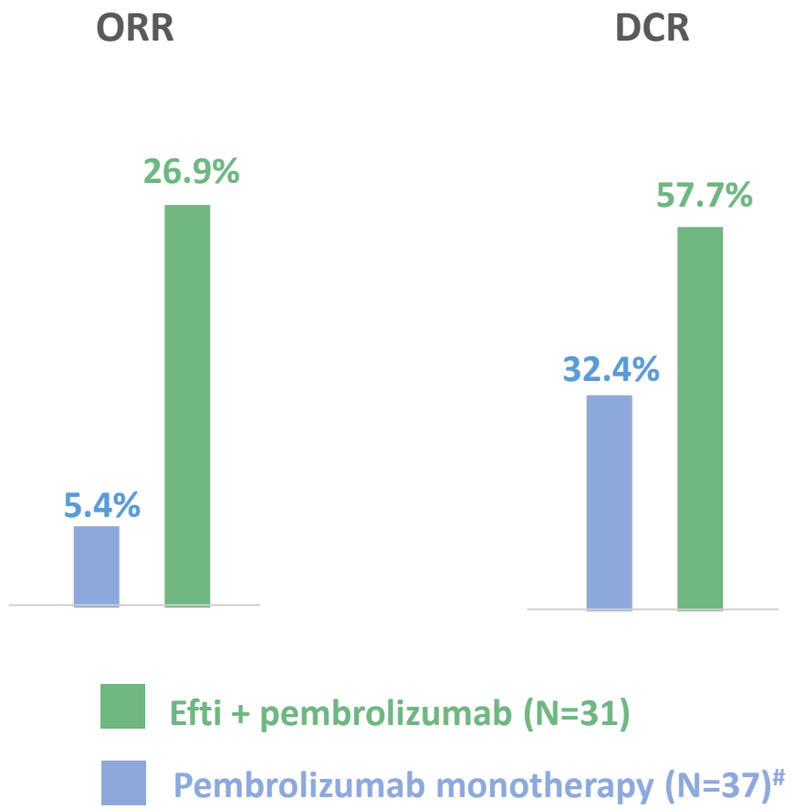
Data cut-off date: March 11, 2024. * Source: Burtness, B. et al. Pembrolizumab Alone or With Chemotherapy for Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma in KEYNOTE-048: Subgroup Analysis by Programmed Death Ligand-1 Combined Positive Score. Journal of Clinical Oncology 2022 40:21, 2321-2332 . CI = Confidence Interval

# Results for Patients with Negative PD-L1 (Cohort B)

## TACTI-003, Cohort B (CPS <1)

- ✓ Positive preliminary 26.9% ORR and 57.7% disease control rate from 26 evaluable patients with CPS <1 reported in April 2024
- ✓ Compares favorably to historical results from KEYTRUDA monotherapy (see figures on the right)

**ORR in CPS <1 has substantially improved and will be presented at an ESMO Virtual Plenary session on 11 July 2024.**






Comparison of data is from different clinical trials. # Data for pembrolizumab monotherapy from KN-048 (https://ascopubs.org/doi/10.1200/JCO.21.02198) in 37 evaluable patients with negative PD-L1 expression (CPS <1). DCR calculated by patients with responses (partial or complete) and stable disease. Pembrolizumab monotherapy approved for 1L HNSCC patients with CPS ≥1 and pembrolizumab with chemo approved for 1L HNSCC in all-comer PD-L1 population. FDA approval based on KN-048.

ESMO VIRTUAL PLENARY

## Cohort B – ESMO Plenary Session in July 2024

- ESMO Virtual Plenaries are monthly presentations of the latest, original scientific data, including *“Phase II trials which demonstrate remarkable therapeutic benefit, scientific insight or progress in an area of unmet need”*
- Updated clinical data from Cohort B in patients with negative PD-L1 expression has been accepted for an ESMO Virtual Plenary session and will be delivered via an oral presentation on 11 July 2024

# Summary & Next Steps

## Summary

- Efti + KEYTRUDA leads to an ORR consistently above 30% across all CPS expression levels (high, low, negative)
- In the randomised Cohort A, efti in combination with KEYTRUDA shows the strongest performance in patients with high PD-L1 expression (CPS ≥20) with a 31.0% ORR as compared to 18.5% for KEYTRUDA monotherapy
- In patients with negative PD-L1 expression (CPS <1, Cohort B), a patient population with no effective chemotherapy-free options and for who KEYTRUDA alone does not work, the IO combination's high response rate is exceptional for a chemo-free regimen
- This effect of efti on anti-PD-1 ⟶ meaning inducing responses in PD-L1 negative tumors where anti-PD-1 are typically primary resistant ⟶ has been observed across multiple diseases (e.g. non-small cell lung cancer, head and neck cancer, melanoma)

## Next Steps

- In addition to the ESMO Virtual Plenary session on 11th July for Cohort B, more clinical data from Cohort A & B in TACTI-003 will be presented next at a medical conference in H2 CY2024
- Based on the positive topline results, the Company will discuss the path forward in 1L HNSCC with regulatory agencies

# Lead Indication

## First Line Non-Small Cell Lung Cancer (NSCLC)

**ASCO 2022 - Dr. Enriqueta Felip** presenting 1L NSCLC data from TACTI-002/KN-798 in Oral Presentation


**SITC 2022 - Dr. Wade Iams** presenting 1L NSCLC data from TACTI-002/KN-798 in Late Breaking Abstract Oral Presentation


**ESMO 2023 - Dr. Enric Carcereny** presenting Overall Survival data in 1L NSCLC from TACTI-002/KN-798

# Immutep & Merck (MSD) to Undertake Phase III Trial in NSCLC

*Opportunity to set a new standard of care across entire NSCLC population regardless of PD-L1 expression*

## MSD / Immutep Collaboration

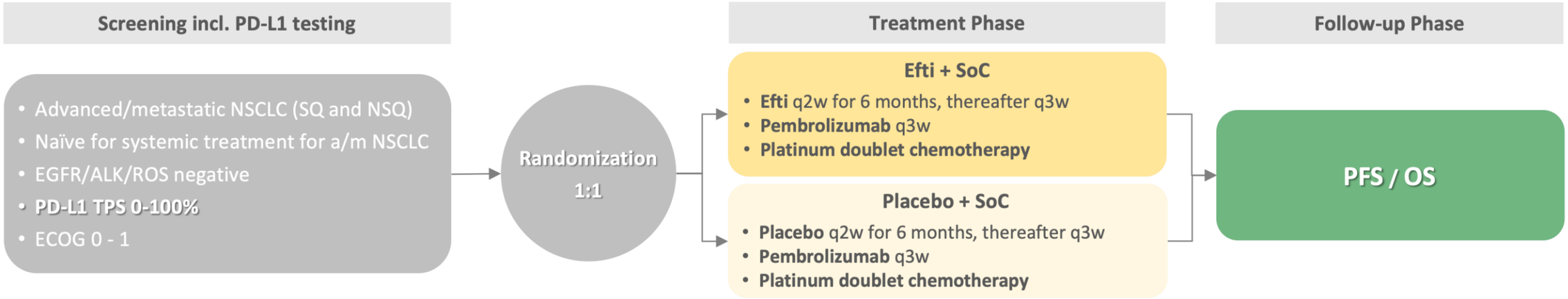
- Immutep will conduct the registrational TACTI-004 Phase III trial and MSD will supply KEYTRUDA
- Agreement enables Immutep and MSD to seek marketing authorisation of the combination and to market their respective compounds with a relevant label indication
- Both parties retain the commercial rights to their respective compounds and are free to conduct other clinical studies, either individually or in combination, in any therapeutic area

## Key Highlights

- All comer trial: will not select for PD-L1 and include both squamous / non-squamous tumors → anticipate fast enrollment
- Trial design has been agreed with all important stakeholders: regulatory agencies across the globe (e.g. FDA, EU based authorities), investigators, MSD and others → strong support across the board
- Clear unique selling point: novel agonist with strong efficacy & favorable safety in 1L NSCLC and best available SOC control arm → quick to enroll
- Success will lead efti directly into a multi-billion market opportunity that exists today for KEYTRUDA in metastatic non-small cell lung cancer

# TACTI-004 Trial Design

## TACTI-004 / KEYNOTE-PNC-91 Trial Design



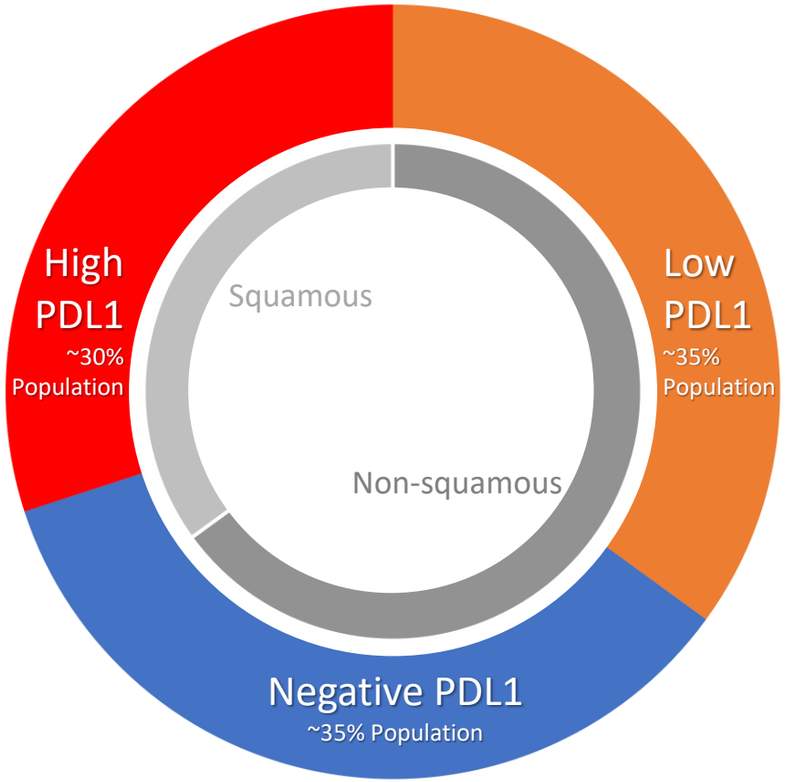

### Trial Overview:

- TACTI-004 will be a 1:1 randomized, double-blind, multinational, controlled clinical study with ~750 patients
- Trial will enroll first line squamous and non-squamous NSCLC patients who are unselected for PD-L1 expression
- Dual primary endpoints will be Progression-Free and Overall Survival with both being adequately powered
- First patient expected to be enrolled in Q4 2024 / Q1 2025
- Futility analysis expected in late 2025 / early 2026 and interim analysis in late 2026 till mid-2027 (event driven)


* Timelines are indicative and subject to change

# Uniquely Positioned Phase III in 1L NSCLC Landscape

- KEYTRUDA has revolutionized the treatment landscape in lung cancer, and as a result MSD (Merck) captures between 7 to 8 of every 10 metastatic lung cancer patients today*
- Of KEYTRUDA's ~US$ 25 billion in sales in 2023, it is estimated that ~US$ 9 billion or +35% are from lung cancer**
- Efti in combination with KEYTRUDA and chemotherapy is uniquely positioned to potential drive a new standard of care for the vast majority of the 1L NSCLC population




TACTI-004 among the few global Phase III trials evaluating combination therapies with KEYTRUDA that addresses almost the entire 1L NSCLC patient population eligible for anti-PD-(L)1 therapy


* MSD Investor Event at ASCO 2024. ** Source of sales figures: Bloomberg, Wall Street research reports and Company reports

# Outlook

## Milestones & Catalysts Ahead

- **Non-Small Cell Lung Cancer –** TACTI-004 preparations for study start with FPI in late 2024 / early 2025
- **Head & Neck Squamous Cell Carcinoma –** Updated Cohort B data 11th July at ESMO Plenary Session; additional data at medical conference H2 2024
- **Non-Small Cell Lung Cancer –** Update from triple combo INSIGHT-003 trial
- **Soft Tissue Sarcoma –** Update from investigator-initiated EFTISARC-NEO study
- **Metastatic Breast Cancer –** Update from AIPAC-003 study evaluating 90mg vs 30mg efti dosing
- **Metastatic Urothelial Carcinoma –** Update from investigator-initiated INSIGHT-005 study
- **Autoimmune Diseases –** Continue IND-enabling studies of IMP761 and move toward to clinic in mid-2024
- **Other indications –** Updates from partnered programs and potential expansion of clinical trial pipeline
- **Cash Balance –** Pro forma cash balance of ~$195 million (US$ ~130 million)[1] providing cash runway to late CY2026



1. Based on cash balance as at 31 March 2024 and assuming completion of a capital raising of A$100.2 million, excluding offer costs; estimate of US$ 130 million based on USD/AUD of $1.506

# Thank you